

## Introduction

SARS-COV-2 (COVID-19) has led to the greatest pandemic in the past century and has resulted in loss of life for hundreds of thousands of individuals. Patients struggling with COVID-19 are increased risk for delirium due to factors such as CNS invasion, inflammatory mediators, organ failure, sedation, ventilation. Psychiatric symptoms of COVID-19 infection range widely, from hyperactivity and agitation, to catatonia and stupor.

### Described Symptoms of COVID-19 Delirium

Mutism	Agitation
Alogia	Confusion
Rigidity	Myoclonus
Abulia	Impulsivity
Rigidity	

Through the early stages of the pandemic, testing administration and processing lacked standardization due to the novel nature and scope of COVID-19. This led to false negative results in asymptomatic patients, who later became symptomatic with COVID-19 infection, despite PCR test.

## Case 1

- 61 year old male with HIV, DMII, HTN, dementia, bipolar disorder and schizophrenia admitted from nursing facility with altered mental status. On Haloperidol 10 mg three times a day, olanzapine 30 mg at bedtime and escitalopram 10 mg. Tested negative for COVID-19 by nasal swab.
- Appeared agitated with repetitive movements, posturing (holding his hands near his face, holding his breath and staring ahead). Yelled out "Help me!" Demonstrated waxy flexibility and automatic obedience. Underwent lorazepam trial of 2 mg QID IV, initially had limited improvement. Olanzapine was reduced to 10 mg at bedtime and haloperidol was reduced to 10 mg twice a day, eventually both stopped.
- Three days later was tested for COVID-19 again and was positive.
- Was tried on valproic acid with improvement (Max dose 500 mg TID)
- Died due to respiratory depression.

### Case 1 Symptoms of Catatonia

Excitable	Posturing
Yelling out "help!"	Waxy flexibility
Automatic obedience	Gegenhalten
Verbigeration	Impulsivity
Rigidity	Violence

## Case 2

- 71 year old male with myasthenia gravis, major depressive disorder, and MCI, admitted for gastrointestinal bleed, with psychiatry consulted for delirium. He received a COVID nasal swab on admission, which was negative.
- On evaluation, the patient was not interactive, demonstrated psychomotor retardation and rigidity, and would not communicate. When evaluated later, there was noted verbigeration, echolalia, and ambitendency. Nursing staff noted impulsivity and excitement overnight.
- Responded well to Ativan challenge, and BFCS decreased from 24 to 4 in 24 hours.
- However, symptoms then worsened despite Ativan titration. He was retested for COVID in light of impending inpatient psychiatry transfer, and tested positive via 2 nasal swabs. Inpatient psychiatry transfer was cancelled.
- Eventually, he was switched to amantadine and Namenda, with good effect. He was discharged to a skilled nursing facility in stable condition.

### Case 2 Symptoms of Catatonia

Stupor	Negativism
Mutism	Withdrawal
Echolalia	Gegenhalten
Verbigeration	Ambitendency
Rigidity	Impulsivity

## Discussion

With the onset of the COVID-19 pandemic, multiple neuropsychiatric manifestations of COVID-19 infection have been reported, including catatonia... We theorize based on previous theories about pathology the following:

### Dr. Maldonado's (2013) theorized Neurochemical mechanisms:

Table 3  
Theorized neurochemical mechanisms associated with conditions leading to delirium  
Data from Maldonado JR. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. Am J Geriatr Psychiatry 2013;21:1190-222; and Maldonado J. Delirium pathophysiology: current understanding of the neurobiology of acute brain failure. Int J Geriatr Psychiatry, in press.

Delirium Source	ACH	DA	GLU	GABA	5HT	NE	TRP	MEL	Phe	His	Cytok	HPA Axis	Cort	NMDA activity	RBF	Inflam	EEG
Anoxia or hypoxia	↓	↑	↑	↑	↓	↓	↓	↓	↑	↑	↑	↑	↑	↑	↑	↑	↓
Aging	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
TBI	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
CVA	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Hepatic encephalopathy	↔	↓	↑	↑	↑	↓	↓	↓	↑	↑	↑	↑	↑	↑	↑	↑	↓
Sleep deprivation	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Trauma, Sx, & Postoperative	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
ETOH & CNS-Dep withdrawal	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Infection or sepsis	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Dehydration & electrolyte imbalance	↔	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Medical illness	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓

### Our theory of Neurochemical mechanism:

Delirium Source	ACH	DA	GLU	GABA	5HT	NE	TRP	MEL	PHE	HIS	Cyto	HPA Axis	COR T	NM DA Acti	RBF	Infla	EEG
COVID 19	↓	↓	↑	↑	↓	↓	↓	↓	↑	↑	↑	↑	↑	↑	↑	↑	↑

## Conclusion

In the cases described, catatonic symptoms appear to be a "herald" for an active COVID-19 infection, even when viral load is too low to be picked up by PCR test. The cases argue for repeated and frequent testing of patients with catatonic symptoms at risk for COVID-19 infection, especially when no primary medical or psychiatric etiology has been identified. **References available upon request.**